

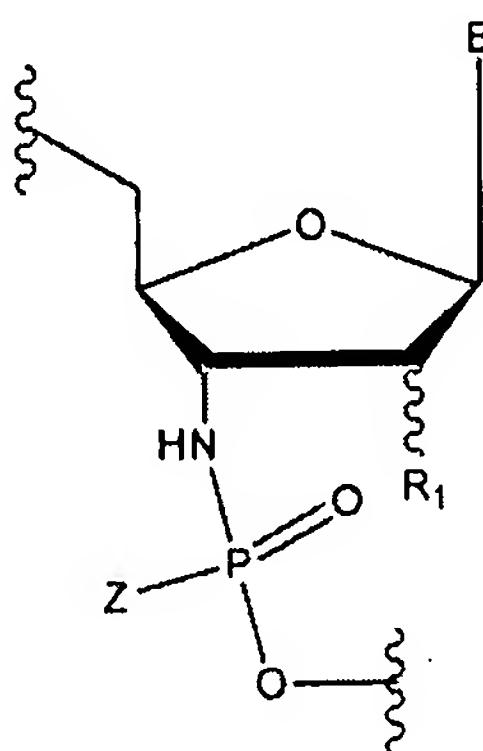
Amendments to the Claims:

This listing of claims will replace all prior versions, and listings of claims in the application:

Listing of Claims:

1-41. (Canceled)

42. (Currently amended) An isolated small double stranded interfering RNA (siRNA) wherein one strand is comprising 15-25 nucleotides complementary to a target nucleic acid sequence and both strands are from 19 to 25 nucleotides in length, and wherein at least one strand of the RNA comprises at least 80% nucleotides one nucleotide of formula:



wherein R₁ is chosen from fluorine and OR₂, R₂ is chosen from hydrogen and lower alkyl, B is chosen from purines, pyrimidines, and analogs thereof, and Z is sulfur.

43. (Previously presented) The small interfering RNA according to Claim 42, wherein all of the internucleoside linkages are ribo N3'→P5' thiophosphoramidate (NPS) linkages.

44. (Canceled)

45. (Previously presented) The small interfering RNA according to Claim 42, wherein the RNA further comprises at least one covalently conjugated lipid moiety.

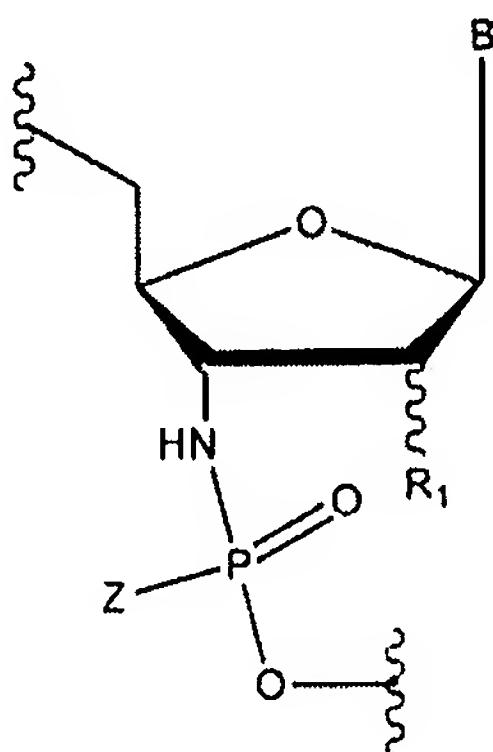
46. (Currently amended) The small interfering RNA according to Claim 45, wherein one the lipid moiety is covalently conjugated to the 5' or 3' terminus of at least one strand of the double-stranded -the RNA, and the lipid moiety is chosen from fatty acids, sterols and hydrocarbons.

47. (Currently amended) The small interfering RNA according to claim 45, wherein at least one strand comprises comprising the structure:

$O-(x-L)_n$

wherein

- O is an oligonucleotide of formula:



wherein R_1 is chosen from fluorine and OR_2 , R_2 is chosen from hydrogen and lower alkyl, B is chosen from purines, pyrimidines, and analogs thereof, and Z is sulfur, and further wherein the oligonucleotide comprises a sequence of 19 [[15]] to 25 bases, and said sequence is at least partially complementary to a selected target sequence;

-L is a lipid moiety;

-x is an optional linker; and

- n is an integer ranging from 1 to 5, wherein if $n > 1$, each additional (x-L) component may be, independently, the same or different.

48. (Previously presented) The small interfering RNA according to Claim 47, wherein L is a lipid chosen from substituted and unsubstituted fatty acids and sterols; or wherein L is chosen from substituted and unsubstituted hydrocarbons.

49. (Previously presented) The small interfering RNA according to claim 48, wherein L is chosen from fatty acids substituted with at least one fluorine; or wherein L is chosen from hydrocarbons substituted with at least one fluorine.

50. (Previously presented) The small interfering RNA according to claim 42, wherein at least 60% of the nucleobases in the oligonucleotide are ribonucleobases.

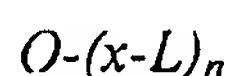
51. (Canceled)

52. *(Withdrawn) A method for effecting the post-transcriptional silencing of at least one gene, comprising administering to a mammal in need of such post-transcriptional silencing at least one small interfering RNA comprising 15-25 nucleotides complementary to a target nucleic acid sequence, wherein the RNA comprises at least one internucleoside linkage chosen from ribo-N3'→P5' phosphoramidate (NP) and ribo N3'→P5' thiophosphoramidate (NPS) linkages.*

53. *(Withdrawn) The method of Claim 52, wherein the small interfering RNA further comprises at least one covalently conjugated lipid moiety.*

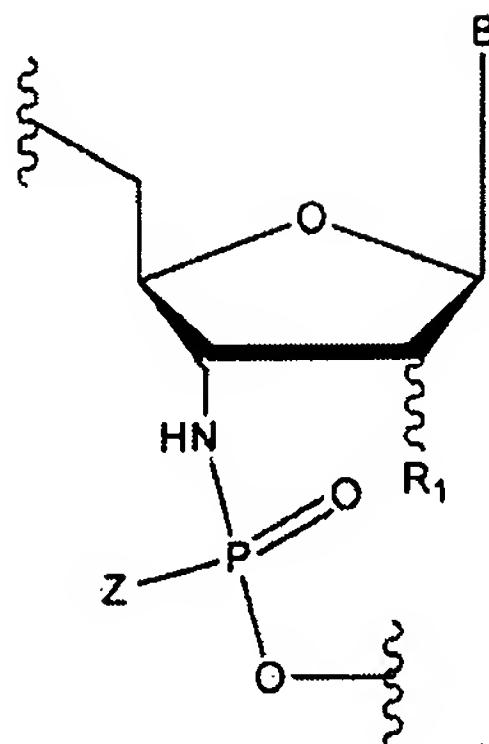
54. *(Withdrawn) The method of Claim 52, wherein the at least one gene encodes at least one mRNA chosen from cellular mRNAs and viral mRNAs; or wherein the at least one gene is an oncogene; or wherein the at least one gene is a viral gene.*

55. *(Withdrawn) A method for effecting the post-transcriptional silencing of at least one gene, comprising administering to a mammal in need of such post-transcriptional silencing at least one compound comprising the structure:*



wherein

-O is an oligonucleotide of formula:



wherein R₁ is chosen from fluorine and OR₂, R₂ is chosen from hydrogen and lower alkyl, B is chosen from purines, pyrimidines, and analogs thereof, and Z is chosen from oxygen and sulfur, and further wherein the oligonucleotide comprises a sequence of 15 to 25 bases, and said sequence is at least partially complementary to a selected target sequence;

-L is a lipid moiety;

-x is an optional linker; and

- n is an integer ranging from 1 to 5, wherein if n>1, each additional (x-L) component may be, independently, the same or different.

56. (Withdrawn) The method according to claim 55, wherein the at least one gene encodes at least one mRNA chosen from cellular mRNAs and viral mRNAs; or wherein the at least one gene is an oncogene; or wherein the at least one gene is a viral gene.

57.-62. (Canceled)

63. (Previously presented) A small interfering RNA as recited in claim 42 wherein said target nucleic acid sequence is a human immunodeficiency virus (HIV) gene, such that said siRNA modulates expression of said HIV gene.

64. – 74. (Canceled)

75. (Previously presented) The compound according to Claim 47, wherein n = 1 and the (x-L) component is covalently conjugated to the 5' terminus of the oligonucleotide O.

76. (Previously presented) The compound according to Claim 47, wherein n = 1 and the (x-L) component is covalently conjugated to the 3' terminus of the oligonucleotide O.

77. (Previously presented) The compound according to Claim 47, wherein n = 2, one (x-L) component is covalently conjugated to the 5' terminus and one independently chosen (x-L) component is covalently conjugated to the 3' terminus.

78. (Canceled)

79. (Canceled)

80. (Previously presented) A composition comprising at least one small interfering RNA according to claim 42 in an amount effective to modulate the expression of at least one gene.